UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/349,954	07/08/99	HAYWARD N	10441Z

HM22/1004

SCULLY SCOTT MURPHY & PRESSER
400 GARDEN CITY PLAZA
GARDEN CITY NY 11530

EXAMINER	
SAOUD, C	
ART UNIT	**PAPER NUMBER**
1647	7

DATE MAILED: 10/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/349,954	Applicant(s) HAYWARD et al.
	Examiner Christine Saoud	Group Art Unit 1647

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *26-28, 30, 43, and 44* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *26-28, 30, 43, and 44* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☒ received in Application No. (Series Code/Serial Number) *08/765,588* .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3 and 4*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Status of Claims

1. Claims 1-25, 29, and 31-42 have been canceled, claims 26-28 and 30 have been amended, and claims 43-44 have been added as requested in paper #2, filed 14 August 1999. Claims 26-28, 30 and 43-44 are pending in the instant application.

Oath/Declaration

2. The Declaration is objected to because it has an address for the inventor Gunther Weber which is illegible. It appears that the Post Office Address was corrected with correction fluid, but the previous address is showing through, which makes the correct address illegible. Correction is necessary.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 08/765,588, filed on 25 April 1997.

Drawings

4. Figure 8 of the instant application is presented on separate pages. Although Figures 8A and 8B are correctly labeled according to 37 C.F.R. § 1.84 (U)(1), which requires that when

partial views of a drawing which are intended to form one complete view must be identified by the same number followed by a capital letter, the Brief Description of the Drawings at page 10 does not properly refer to the Figures, in that lower case letters are used. Correction is required.

Figures 1-6, 9-11, and 16-17 of the instant application are presented in separate panels or on separate pages. 37 C.F.R. § 1.84(u) (1) states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the **same number followed by a capital letter**. The instant application uses the format of a number followed by lower case roman numerals. Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(u) (1), the specification should be amended to change the Brief Description of the Drawings and the rest of the specification accordingly. If, for example, Figure 1 is divided into Figures 1A, 1B, 1C, and 1D, then the Brief Description and all references to this figure in the specification must refer to Figures 1A, 1B, 1C and/or 1D.

Specification

5. The title of the invention is not descriptive (i.e. "Novel growth factor ..."). A new title is required that is clearly indicative of the invention to which the claims are directed.

6. Applicant has submitted a new paper copy of the Sequence Listing and provided an amendment directing its entry into the instant specification. However, Applicant neglected to

cancel the previous copy of the Sequence Listing. Applicant should include an amendment in the next response which requests the cancellation of the previous copy of the Sequence Listing.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 26-28, 30, 43-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acid molecule of SEQ ID NO:5 or encoding a polypeptide having the amino acid sequence of SEQ ID NO:6, does not reasonably provide enablement for nucleic acid molecules which encode a polypeptide comprising an amino acid sequence having at least about 70% similarity to SEQ ID NO:6, or for a nucleic acid which has at least about 70% similarity to SEQ ID NO:5 or hybridizes under low stringency conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The application discloses a nucleic acid molecule which is differentially spliced to provide for several VEGF-like molecules. These VEGF-like proteins have the amino acid sequences of SEQ ID NO:4, 6, 8, and 10. The instant specification does not provide for modification of these proteins or nucleic acid molecules encoding these proteins. The specification contemplates any VEGF molecule which differs from the prior art molecule known as VEGF165 in stating "the

molecule of the present invention is VEGF-like or is a homologue of VEGF but comprises an amino acid sequence which is similar but non-identical to the amino acid sequence of VEGF" (see specification at page 4). Embodiments which are included in this definition are species variants, mammalian as well as birds, fish, and reptiles. However, the instant specification fails to provide representative examples which would enable such breadth as what is intended by the specification or by the claims directed to nucleic acids encoding a polypeptide comprising at least about 70% similarity to SEQ ID NO:6. Applicant is in essence attempting to claim molecules which have not been made or described in the instant specification. The fact that one of ordinary skill in the art could make a molecule which shares sequence identity to the disclosed sequences is irrelevant because one would not have a reasonable expectation that those molecules which are made would function in the manner required in order to use the molecules. The instant specification provides no guidance as how to modify the disclosed proteins and obtain a protein which has the biological activity of VEGF and no guidance as to which amino acids (i.e. structural elements) of the native proteins are critical to the biological activity. Without this type of guidance, the skilled artisan does not have a reasonable expectation of mutating the polypeptide of SEQ ID NO:6 or the nucleic acid molecule of SEQ ID NO:5 and obtaining a functional protein that retains a biological activity of the native protein, absent evidence to the contrary. One may argue screening for bioactivity could be done, however, this is basically a "wish to know" and the standard for an enabling disclosure is not one of making and testing. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function

in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not without actually making and testing them, then the instant application does not support the breadth of the claims.

A review of *In re Wands* clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the enablement of an invention. The claims encompass a limitless number of embodiments because they recite no structural limitations on the polypeptide due to the recitation of at least about 70% similarity, which does not even require identical amino acids (factor 1). The specification provides no guidance as to amino acid positions and/or regions which would provide the recited bioactivity of VEGF (factor 2) and provides no examples of any VEGF polypeptides other than the native protein (factor 3). Additionally, the specification provides no molecules which differ by as much as the contemplated 30% and still retain biological activity other than naturally occurring proteins. The claims are exceedingly broad because they only require at least about 70% similarity, which means that not a single amino acid need be the same, but only similar (factor 8). In addition, although the skill in the art is known to be high (factor 6), the results of mutating amino acids to produce a function protein is highly unpredictable (factors 4, 5 and 7). Therefore, in light of this

analysis, one would reasonably conclude that the breadth of the instant claims is not commensurate in scope with the specification, absent evidence to the contrary.

Claim 44 is directed to a method of making a protein using a nucleic acid molecule that "hybridizes under low stringency conditions to a reverse complement of the nucleotide sequence of SEQ ID NO:5". However, there is no limitation in the claim that requires the hybridizing sequence to encode a protein. There are a multitude of sequences that would be capable of hybridizing to the disclosed sequence under low stringency conditions, but they would not be useful in a method of making a protein unless they actually encoded a protein. Furthermore, the instant specification fails to teach how to make a protein with a nucleic acid molecule that does not encode a protein. Therefore, the instant claim is not enabled for the claimed breadth for the reasons provided.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 26-28, 30 and 43-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 is directed to a nucleic acid "complementary to a sequence", however, the nucleic acid is complementary to another nucleic acid, and not the "sequence" because the sequence is only a representation of the molecule on paper. The claim should be directed to a

nucleic acid which is complementary to a nucleic acid which encodes the polypeptide. Therefore, the claim is indefinite. Claim 44 also requires hybridization to a sequence; this grounds of rejection could also be avoided in this claim by hybridizing to the nucleic acid and not the "sequence".

11. Claims 26 and 43-44 recite "at least about 70% similarity", however, it is not clear what lower limit is intended by the claims. Is the lower limit 70% or some other value? Therefore, the claims are indefinite because the metes and bounds of "at least about 70%" cannot be determined.

12. Claim 44 recites a nucleic acid which "hybridizes under low stringency conditions". There are several factors which affect the hybridization of nucleic acid molecules and there are a multitude of conditions which may or may not be considered stringent because stringency is a relative condition. Without some sort of guidance or definition in the claims of what this term is meant to encompass, the metes and bounds of the claims cannot be determined, thereby making the claims indefinite.

Double Patenting

13. Claims 26-28, 30 and 43-44 of this application conflict with claims 28, 30, 33, 44-47, and 50-51 of Application No. 08/765,588. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the

conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 26-28, 30 and 43-44 are provisionally rejected under the judicially created doctrine of double patenting over claims 28, 30, 33, 44-47, and 50-51 of copending Application No. 08/765,588. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: nucleic acids encoding VEGF-like molecules, wherein the VEGF-like molecule has the amino acid sequence of SEQ ID NO:6 or similarity thereto. It is noted that the claims are in flux, and it is not clear that the claims in '588 do not conflict with the instant claims.

Applicant should explain why the instant claims are not encompassed by the claims of '588 or cancel the conflicting material from all but one application or submit a terminal disclaimer in one of the applications.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Conclusion

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556. If this number is out of service, please call the Group receptionist for an alternate number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

October 2, 2000

CHRISTINE SAOUD
PATENT EXAMINER

Christine Saoud